Title:

The Appropriateness of Antibiotic Prescriptions in Community-Acquired Acute Pediatric Respiratory Infections in Spanish Emergency Rooms.

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ABSTRACT

Objective: To describe the variability and evaluation of the appropriateness of antibiotic prescriptions in community-acquired respiratory infections (ARI) during childhood in Spain.

Methods: A descriptive, multicenter study of variability in clinical practice was carried out, by evaluating a prospective series of pediatric patients attended in the emergency rooms of 11 Spanish hospitals and diagnosed with community-acquired ARI. The appropriateness of the antibiotic prescriptions was assessed by comparing our clinical practice with consensus guidelines developed for this study.

Results: We collected data from 6,249 ARI emergencies studied on 30 separate days. Antibiotics were prescribed in 58.7% of the ARI (bronchiolitis: 11.5%, bronchitis: 40.2%, pharyngotonsillitis: 80.9%, non-specified ARI: 34.8%, pneumonia: 92.4%, otitis: 93.4%, sinusitis 92.6%). The most commonly used antibiotics were amoxicillin-clavulanate (33.2%), amoxicillin (30.2%), cefuroxime axetil (8.5%) and azithromycin (6%). According to the consensus guidelines developed for this study, therapy was considered to be appropriate in 63.1% of the ARI (first choice: 52.1%; alternative choice: 11.0%) and inappropriate in 36.9%. The percentages of inappropriate prescription according to ARI groups were: bronchiolitis: 11.5%, bronchitis: 31.5%, pharyngotonsillitis: 54.8%, non-specified ARI: 34.7%, pneumonia: 13.9%, otitis: 25.6% and sinusitis: 22.2%.

Conclusions: There is excessive use of antibiotics in acute respiratory infections which are supposedly viral in origin. An important number of ARI of potentially bacterial origin are treated with antibiotics which are not sufficiently efficacious or which have a broader spectrum than necessary.

Key Words: Antibiotics, acute respiratory infection, variability, clinical practice, appropriateness, drug utilization study.

INTRODUCTION

Acute respiratory infections (ARI) are the most frequent infectious diseases in childhood [1-5] and the main reason for antibiotic prescriptions[6], which are justified in only a small percentage of ARI [7-14].

Diagnosis and therapeutic management of ARI in daily clinical practice is generally based on subjective evaluation. The decision to begin empirical anti-infectious treatment is based on the initial diagnosis, the most likely etiology and the usual antimicrobial susceptibility of the suspected pathogens. In most cases, the suitability of diagnosis and treatment can only be evaluated by the subjective assessment of the clinical response. Certain conditioning factors can also influence therapy. These include lack of continued medical education for some physicians, the increasingly widespread use of defensive medicine and marketing by pharmaceutical companies.

The excessive use of antibiotics is considered the most important reason for development of bacterial resistances to antimicrobial drugs[15-16], which is an important public health problem in both in Spain and in many other countries [17-22].

To evaluate variability and appropriateness of antibiotic prescriptions for ARI in Spain, we reviewed ARI in pediatric patients attended in the emergency rooms of a group of hospitals in different areas of Spain.

METHODS

We carried out a descriptive multicenter cross-sectional study on the variability and appropriateness of the prescription of antibiotics in children with ARI. The study population was made up of pediatric patients (0-18 years old) attended in the emergency services of eleven Spanish hospitals, over a 6-month period (January to June 1997): Hospital La Paz, Madrid; Hospital Vall d'Hebron, Barcelona; Hospital Xeral-CIES, Vigo; Hospital de Cabueñes, Gijón ; Hospital Marqués de Valdecilla, Santander; Hospital General Básico, Ronda; Hospital General, Soria; Hospital Dr. Peset, Valencia; Hospital Universitario, Valladolid; Hospital Virgen de la Concha, Zamora; Hospital de Medina del Campo, Valladolid.

We drew up reference standards for antibiotic prescriptions in ARI following the methodology of the Consensus Conferences[23] . These standards were used to assess the appropriateness of these prescriptions.

Estimation of ARI sample size was made using Epiinfo 6.04a, in order to obtain a precision of ±2% (95% confidence level) in the estimation of the global appropriateness percentage (min size = 2,400 cases) and ±4% by ARI subgroups (min size = 600 cases). We performed a cluster random sampling (one cluster = all ARI on each day) by applying the sampling unit to every day of the six-month period. We selected 30 days using computer-generated random numbers.

A physician from outside the emergency services completed a record for each patient in which the following information was recorded: age, sex, history of allergy to antibiotics, diagnosis (according to ICD 9 CM), comorbidity, previous antibiotherapy, type of antimicrobial treatment and route of administration, hospital admission or discharge and type of prescribing doctor (resident, pediatrician, other). In all cases, we only considered the information available from the emergency room.

We reviewed published studies on the treatment of ARI, basing efficacy on clinical trials, cost-effectiveness and safety. This information was summarized in a document[24], and used to generate questions related to the treatment of ARI, which would later be addressed by a panel of experts.

Following the methodology of the Consensus Conferences of the U.S. National Institutes of Health[23], a panel of experts was set up which issued recommendations on treatments that were considered as first choice, alternative and inappropriate for each ARI. The recommendations were classified using a hierarchical system where scientific evidence was grouped as EVIDENCE A (well demonstrated scientific evidence based on controlled clinical trials), EVIDENCE B (suggested by uncontrolled studies or studies carried out in a different population; epidemiological information on microorganisms and resistance) or EVIDENCE C (based on the opinion of experts)[25]. The prescriptions were classified on the basis of their adherence to these recommendations (Table 1)[24].

We excluded from the analysis of appropriateness and variability the following diagnoses: external otitis, mastoiditis, epiglottitis and pulmonary tuberculosis. Additionally, we excluded patients with acquired or congenital immunodeficiency.

ARI were grouped for the analysis of variability and appropriateness into the following categories: 1) bronchiolitis, 2) acute bronchitis ,3) pharyngotonsillitis, 4) croup - influenza-common cold and non-specified or multiple acute respiratory infections, 5) pneumonia, 6) acute otitis media and 7) acute sinusitis.

Statistical analysis.

The frequencies of first choice, alternative and inappropriate prescriptions were qualified both globally and according to hospital. The variability of the appropriateness of the prescription between hospitals was estimated by means of the chi square test and exact tests. The weighted percentages of first choice prescription/inappropriate use were calculated with 95% confidence intervals (95% CI), according to models of randomized effects[26]. Nonparametric tests (Mann Whitney and Spearman's correlation coefficient) were used to contrast the grouped data of appropriateness in the different centers. Finally, we estimated the contribution to appropriateness of prescriptions for the variables hospital, comorbidity, admission, previous antibiotherapy, prescribing doctor, age and type of ARI using multiple non-conditional logistic regression. All the variables were coded to evaluate the effect of each category on the mean effect. The modeling strategy to select variables was “forward stepwise” using changes in the likelihood ratio.

RESULTS

We evaluated 29,436 emergency room visits collected from the 30 study days. Of these, 6,098 were ARI (20.71%; 95%CI: 20.25-21.18). We collected 151 additional ARI during the days that followed the selected period to complete a valid sample size of five ARI per day per hospital. Once the registers were purged, we obtained a final sample size of 6,249 ARI which were valid for analysis. Mean patient age was 3.65 years (SD: 3.23; range: 1 month-18 years), more than half were under 3 years old and 80 % under 6 years old. Only 5.4% were admitted to hospital. Table 2 shows an analysis of frequency of other variables .

An antibiotic was prescribed in 58.5% of all of the ARI with important differences among the participating centers (range: 37.4%-84.7%). When we considered the specific ARI, the percentages varied from 93.4% in otitis to 11.5% in bronchiolitis. Table 3 shows the most frequent prescriptions according to the different groups of ARI. The most commonly prescribed antibiotics were amoxicillin-clavulanate, amoxicillin, cefuroxime and azithromycin.

There were significant differences among the hospitals related to the prescribed antibiotics ($p<0.0001$). The percentage ranges in antibiotic prescription were 4.3%-27.6% for amoxicillin-clavulanate, 4.8%-26.2% for amoxicillin, 0.6%-16.4% for cefuroxime and 0%-13% for azithromycin.

Management of the ARI was empirical except in eleven cases (0.18%) for which microbiological information was obtained (9 pharyngotonsillitis, 1 pneumonia, 1 pulmonary tuberculosis). A culture of a pharyngeal sample or a rapid diagnostic test was performed in 9 out of 1,716 pharyngotonsillitis. The route by which antibiotics were administered was oral in most cases, intramuscular in 79 (1.2%), intravenous in 57 (0.9%) and topical in 18 (0.2%). Previously untreated patients received 76.2% of the prescriptions and the remainder were received by patients already taking antibiotics. The prescription was maintained in 16.0% of cases and changed in 7.7%.

After comparing the suitability of each prescription with the consensus recommendations, the antibiotics prescribed were classified as first choice, alternative or inadequate. The proportion of appropriate prescriptions was 63.1% (first choice: 52.1%; alternative choice: 11.0%), whereas it was 36.9% for inappropriate prescriptions Heterogeneity in the appropriate use of antibiotics between hospitals was significant ($p<0.0001$).

Table 4 shows the percentages for appropriate treatment of specific ARIs. We show the weighted percentage of first choice and inadequate use together with the crude frequencies and percentages. There is a high degree of appropriateness in the treatment of bronchiolitis (no treatment) and acute sinusitis and a lower degree in pharyngotonsillitis and acute bronchitis. The only group with a high percentage of prescriptions for alternative drugs was pneumonia.

We obtained important differences in the degree of appropriateness of prescriptions according to previous antibiotic treatment. The percentage of inappropriate prescriptions was 32% for those with no previous antibiotic treatment, 77.2% for those who maintained the previously administered treatment, and 41.5% for those who changed the previous treatment ($p<0.0001$).

We also found other variables which were significantly associated with the degree of appropriateness such as: hospital admission (inappropriate prescriptions in those who were admitted to hospital were 25.1%, and 37.6% in those who were not admitted to hospital: $p<0.0001$); patient age (inappropriate prescriptions in < 18 months: 32.6%; 18-35 months: 48.1%; ≥36 months: 34.5%, $p<0.0001$) and the prescribing physician (inappropriate prescriptions by residents: 34.6%; pediatricians: 38.5%; emergency room staff physicians who were not pediatricians: 45.8%; $p<0.0001$).

We used multiple logistic regression to calculate the adjusted proportions of first choice and inadequate prescriptions for each center, controlling the existing differences related to comorbidity, hospital admission, prescribing physician, previous treatment with antibiotics, age and type of ARI. The adjusted proportions varied from 31.0 to 69.8% for first choice, and from 13.2 to 54.3% for inadequate use.

Table 5 shows the differences in the crude proportions of appropriateness among hospitals according to whether they were teaching hospitals, hospitals with a pediatric center, hospitals with pediatrics residents in training or hospitals with an independent pediatric emergency room. We also found a positive correlation (Spearman´s correlation coefficient) between first choice percentage prescription and different indicators of hospital activity such as: number of hospital beds (0.67; $p=0.022$), number of hospital pediatric admissions (0.79; $p=0.003$) and the reference population (0.61; $p=0.044$).

DISCUSSION

The study of variability and appropriateness of antibiotic prescription in community-acquired acute respiratory infections in childhood is very important, especially in a health service such as ours which has a high consumption of antibiotics[16,27,28]. This fact has no doubt contributed to our very high rates of bacterial resistance[18,20]. The study of ARI in children is particularly interesting, as they are the most frequent infection and the main indication for antibiotics. In our study, ARI represented more than 20% of hospital emergencies and antibiotics were administered in 60% of cases.

Although this study was carried out in hospitals, we think that the ARI included in our sample do not differ significantly from those attended in primary care[5]. In our health service, hospital emergency rooms attend a high percentage of patients who can be treated in primary care in addition to those who do in fact need hospital attention[29-31]. Therefore, it is no surprise that, in our study, a low number of patients are admitted to hospital and the percentage and distribution of ARI are similar to those observed in primary care[1,5].

Our information collection system (random sampling, retrospective collection from clinical history, with no previous intervention) was aimed at guaranteeing the validity and representativeness of the sample, and took care to avoid circumstantial modifications in prescription patterns and information bias. The hospitals in our study are representative of hospitals in Spain, even though their selection was based on convenience criteria. Our data were collected during two seasons (winter/spring). Although this may bias the number and type of the collected ARI, we do not think that this fact has repercussions on the appropriateness of antibiotic prescriptions.

An analysis of clinical practice frequently reveals a lack of reliable evidence-based medicine[25]. This is also seen in the treatment of the ARI in our study in which more than 40% of treatments were considered as inadequate. In Spain, other series of ARI attended in primary care had similar or slightly lower percentages[5,9,12].

The main cause of inadequate prescription is the use of antibiotics in presumably viral infections. In our study, antibiotics were prescribed to one third of croup – influenza - common cold and non-specified or multiple ARI, 40% of acute bronchitis and in a small percentage of bronchiolitis. The use of antibiotics in these situations is an example of malpractice which is widespread[10,32-35], expensive[36], has no scientific basis whatsoever[37-40], and, above all, leads to the development of resistances[15-20].

We cannot estimate from our study the reasons why antibiotics were used in these presumably viral processes. However, the differences that we found in prescribing profile such as the type of hospital, type of physician or the existence of certain antecedents (previous antibiotic treatment, patient age) suggest that there are some circumstances which could condition the prescription.

The pressure to attend patients experienced by hospital emergency services often forces physicians to solve problems and take decisions very quickly. Some physicians think that an antibiotic prescription can be more effective than diagnostic tests and observation of patient evolution [33]. Furthermore, prescribing an antibiotic takes less time than explaining to the patient why an antibiotic should not be prescribed[41]. Similarly, there is a mistaken idea[36] among some physicians, and especially among patients[42], who think that the use of antibiotics in situations such as the common cold prevents bacterial superinfections and their complications.

In the treatment of other ARI of potential bacterial etiology with specific treatment indications, inadequate prescription is related either to the use of antibiotic treatment which is not sufficiently efficacious against the pathogens responsible, or to the use of antibiotics with a broader spectrum than is necessary.

Our study is limited in that we cannot guarantee the validity of the diagnoses and it is probable that not all of them are rigorous enough. Our objective is not to evaluate the appropriateness of the diagnoses but that of the treatments. We think that this issue affects antibiotic consumption because some physicians turn to certain diagnoses in order to prescribe antibiotics[8].

We found a significant variability in the degree of appropriateness when comparing the different hospitals in our study. This variability could be due to the different characteristics of each hospital (teaching hospitals, general hospitals, pediatric hospitals and county hospitals), the profile of the prescribing physician[32,35] and the existence of different clinical protocols based on local epidemiological characteristics. In our study, teaching hospitals, hospitals with a higher number of beds or population served, pediatric hospitals and hospitals with an independent pediatric emergency room had a higher degree of appropriateness. This suggests that continued medical education may be deficient[35], mainly in non-teaching hospitals where prescriptions are not normally handled by residents or pediatricians.

Our study stresses the need to improve antibiotic prescription in ARI. This can be helped by systematic reviews of the available scientific evidence as well as the preparation and diffusion of clinical practice guides. Studies like ours which do not include additional measures are likely to have little impact. Nevertheless, they are necessary to quantify the magnitude of the problem and to evaluate its evolution.

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Table 1.- Appropriateness criteria in antibiotic prescription by type of ARI (degree of scientific evidence in brackets).

ARI	First choice	Alternative use
Bronchiolitis	No antibiotics (A)	
Acute bronchitis	No antibiotics (B)	Macrolides (C) [a]
Pharyngotonsillitis		
Probable or confirmed *S. pyogenes* Infection	Oral Penicillin V (A) Penicillin Benzatin i.m. (A) β-lactam allergy: Josamycin (C), Miocamycin (C) Erythromycin (C)	Amoxicillin (C) Ampicillin (C) Other macrolids (C) Clindamycin (C)
S. pyogenes infection not probable [b]	No antibiotics (B)	
Bacteriological failure	Amoxicillin-Clavulanate (C) Oral Cephalosporin 2ª generation (C)	Clindamycin (C)
Croup -influenza-common cold and non-specified or multiple ARIs	No antibiotics (A)	
Acute otitis media		
No risk factors	Amoxicillin (A) Amoxicillin-Clavulanate (B) No treatment (in >18 months) (C)	Cefuroxime axetil (C) Cefpodoxime (C) β-lactam allergy Azithromycin (B) Clarithromycin (C) Erythromycin (C)
Risk factors [c]	Amoxicillin-Clavulanate (B)[d]	Amoxicillin (A)[d] Cefuroxime (C) Cefpodoxime (C) β-lactam allergy: Azithromycin (B) Clarithromycin (C) Erythromycin (C) Hospitalized patients: Cefotaxime (B) Ceftriaxone (B)

Table 1 (continuation): Appropriateness criteria in antibiotic prescription by type of ARI (degree of scientific evidence in brackets).

ARI	First Choice	Alternative use
Acute sinusitis	Amoxicillin (C)[d] Amoxicillin-Clavulanate (C)[d] No antibiotics (C)[e]	Cefuroxime (C) Cefpodoxime (C) β-lactam allergy (C): Azithromycin / Clarithromycin Hospitalized patients: Cefotaxime / Ceftriaxone (C)
Pneumonia		
< 3 years Not hospitalized	Amoxicillin-Clavulanate (B)[d]	No antibiotics (B) Amoxicillin (B)[d,f] Cefuroxime axetil (B) Azithromycin (C)[g]
< 3 years Hospitalized	Cefotaxime / Ceftriaxone (B) Amoxicillin-Clavulanate (B)[d]	No antibiotics (B) Penicillin /Ampicillin (B)[d,f] Cefuroxime (B) Erythromycin / Clarithromycin (C)[h]
≥ 3 years Not hospitalized	Macrolides (B)	Amoxicillin (C) Amoxicillin-Clavulanate (C) Cefuroxime axetil (C)
≥ 3 years Hospitalized	Cefotaxime / Ceftriaxone (B) Amoxicillin-Clavulanate (B)[d] And/or Erythromycin / Clarithromycin (C)	Penicillin /Ampicillin (B)[d] Cefuroxime (B)

[a] Alternative in persistent cases (10 days)

[b] Children under 3 years of age or with no clinical and epidemiological signs of streptococcal infection.

[C] Risk factors: Patients with recurrent otitis. Previous and recent antibiotic administration (β-lactam). Otitis being treated but with poor evolution. Kindergarten children under 18 months .

[d] Risk factors for penicillin resistant pneumococcal infection (previous respiratory infections treated with β-lactams and a poor evolution) or intake of high doses of amoxicillin (in combination or alone).

[e] In the absence of local inflammatory signs (facial pain, periorbitary oedema) or general affection.

[f] Patients who have been vaccinated against *H. influenzae*.

[g] β-lactam allergy.

[h] Infant under 6 months with a suspected infection by *Chlamydia trachomatis*.

Table 2.- Global analysis of the main variables frequencies.

Variable	No.	**%**
Sex		
Male	3441	55.1
Female	2769	44.3
Not specified	39	0.6
ARI groups		
Croup -influenza-common cold and non-specified or multiple ARIs [a]	2557	40.9
Pharyngotonsillitis	1716	27.5
Otitis	821	13.1
Bronchitis	531	8.5
Pneumonia	288	4.6
Bronchiolitis	200	3.2
Sinusitis	81	1.3
Other	55	0.9
Level of the prescribing physician		
Resident in Pediatrics	2820	45.1
Resident in other specialty	888	14.2
Pediatricians	734	11.7
Medical staff, not pediatricians	694	11.1
Mixed	19	0.3
Not specified	1094	17.5
Immunodeficiency	13	0.2
Antibiotic allergy [b]	96	1.5
Penicillins and/or Cephalosporins	80	1.3
Macrolides	8	0.1
Comorbidity [c]	336	5.5
Previous antibiotic treatment	1044	16.7

[a] 1397 non-specified or multiple ARI; 911 common cold; 209 croup and 40 influenza.

[b] 4 Simultaneous allergy to macrolids and β-lactams

[C] Asthma:143; Diarrhea-Emesis: 46; Epilepsy-Convulsions:31; Urticaria-Dermatitis-Exanthema: 22; Preterm: 17; Recurrent bronchitis: 16; Renal and urinary tract disease: 16; Neurologic disease:14; Congenital cardiopathies: 12; Pulmonary diseases: 5; Cerebral palsy: 4; HIV infection: 3; Other problems: 7.

Table 3. Groups of antibiotics most frequently prescribed in our series, globally and according to the type of ARI.

Prescriptions	**Total**		**Bronchiolitis**		**Acute Bronchitis**		**Pharingo-tonsillitis**		**Non-specified ARI, Croup Rhinopharingitis Influenzae**		**Pneumonia**		**Acute Otitis**		**Acute Sinusitis**	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
No Antibiotics	2567	(41.3)	177	(88.5)	320	(60.6)	318	(18.6)	1665	(65.3)	21	(7.3)	54	(6.6)	6	(7.4)
Peni/Amoxi/Ampicillin																
Amoxicillin	1113	(17.9)	8	(4.0)	52	(9.8)	579	(33.8)	298	(11.7)	45	(15.7)	126	(15.5)	3	(3.7)
Penicillin	92	(1.5)					85	(5.0)	6	(0.2)	1	(0.3)				
Amoxicillin	16	(0.3)	1	(0.5)	1	(0.2)	2	(0.1)	5	(0.2)	5	(1.7)	2	(0.2)		
Amoxicillin-Clavulanate	1222	(19.7)	2	(1.0)	67	(12.7)	377	(22.0)	310	(12.2)	75	(26.1)	336	(41.2)	47	(58.0)
2nd Gen. Cephalosporins																
Cefuroxime	314	(5.0)	4	(2.0)	23	(4.4)	94	(5.5)	52	(2.0)	34	(11.8)	94	(11.5)	5	(6.2)
Cefaclor	157	(2.5)			9	(1.7)	37	(2.2)	43	(1.7)	6	(2.1)	54	(6.6)	5	(6.2)
Other	13	(0.2)			3	(0.6)	5	(0.3)	4	(0.2)			1	(0.1)		
3rd Gen. Cephalosporins																
Cefixime	92	(1.5)	1	(0.5)	1	(0.2)	33	(1.9)	11	(0.4)	6	(2.1)	40	(4.9)		
Cefotaxime	33	(0.5)	2	(1.0)	6	(1.1)	6	(0.4)	1	(0.0)	14	(4.9)	3	(0.4)	1	(1.2)
Ceftriaxone	14	(0.2)	1	(0.5)	2	(0.4)			1	(0.0)	6	(2.1)	4	(0.5)		
Other	19	(0.3)			2	(0.4)	5	(0.3)	3	(0.1)	2	(0.7)	7	(0.9)		
Erythromycin	87	(1.4)	2	(1.0)	11	(2.1)	24	(1.4)	24	(0.9)	21	(7.3)	4	(0.5)		

Table 3 (continuation). Groups of antibiotics most frequently prescribed in our series, globally and according to the type of ARI.

Prescriptions	Total		Bronchiolitis		Acute Bronchitis		Pharingo-tonsillitis		Non-specified ARI, Croup Rhinopharingitis Influenzae		Pneumonia		Acute Otitis		Acute Sinusitis	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Other macrolides																
Azithromycin	222	(3.6)			16	(3.0)	69	(4.0)	62	(2.4)	15	(5.2)	48	(5.9)	11	(13.6)
Clarithromycin	136	(2.2)	1	(0.5)	9	(1.7)	46	(2.7)	30	(1.2)	23	(8.0)	25	(3.1)	1	(1.2)
Josamycin	22	(0.4)			3	(0.6)	3	(0.2)	5	(0.2)	9	(3.1)	2	(0.2)		
Miocamycin	34	(0.5)			1	(0.2)	18	(1.1)	9	(0.4)	2	(0.7)	4	(0.5)		
Other	3	(0.0)	1	(0.5)	2	(0.2)	1	(0.1)								
Other[a]	62	(1.0)			1	(0.2)	12	(0.7)	19	(0.8)	2	(0.6)	11	(1.3)	2	(2.4)

[a] Includes Cefradoxil (16), C Trimethoprim-sulfamethoxazole (7), Clindamycin (1), Cloxacillin (1), Fosfomycin (1), Rifampicin (1), Trimethoprim (5), topical use (18) and others (11).

Table 4.- Global appropriateness of antibiotic prescription. Absolute and relative (%) frequencies as well as 95% confidence intervals (95%CI) are shown in columns. Significant heterogeneity estimation (p<0.0001).

	First choice			**Alternative use**		**Inadequate use**		
Centers	No.	%	(95%CI)	No.	%	No.	%	(95%CI)
Hospital A	775	72.5%	(69.8-75.2)	53	5.0%	241	22.5%	(20.0-25.0)
Hospital B	592	56.2%	(53.2-59.2)	66	6.3%	395	37.5%	(34.6-40.4)
Hospital C	88	43.6%	(36.7-50.4)	25	12.4%	89	44.1%	(37.2-50.9)
Hospital D	310	46.6%	(42.8-50.4)	72	10.8%	283	42.6%	(38.8-46.3)
Hospital E	241	46.2%	(41.9-50.4)	35	6.7%	246	47.1%	(42.8-51.4)
Hospital F	518	67.1%	(63.8-70.4)	136	17.6%	118	15.3%	(12.7-17.8)
Hospital G	39	26.2%	(19.1-33.2)	19	12.8%	91	61.1%	(53.2-68.9)
Hospital H	284	50.7%	(46.6-54.9)	87	15.5%	189	33.8%	(29.8-37.7)
Hospital I	238	28.1%	(25.1-31.1)	145	17.1%	464	54.8%	(51.4-58.1)
Hospital J	72	44.4%	(36.8-52.1)	24	14.8%	66	40.7%	(33.2-48.3)
Hospital K	50	32.1%	(24.7-39.4)	14	9.0%	92	59.0%	(51.3-66.7)

Table 5.- Appropriateness frequencies and percentages by ARI group. Weighted percentages (with 95% confidence intervals) of first choice and inadequate prescriptions.

	First choice			**Alternative use**		**Inadequate use**		
ARI	No.	(%)	% weighted (95%CI)	No.	(%)	No.	(%)	% weighted (95%CI)
Bronchiolitis	177	(88.5%)	86.3% (68.0-100)			23	(11.5%)	13.6% (0.0-27.6)
Acute bronchitis	320	(60.7%)	40.8% (27.0-54.7)	41	(7.8%)	166	(31.5%)	46.8% (33.1-60.6)
Acute pharyngotonsillitis	391	(22.8%)	22.7% (15.9-29.5)	384	(22.4%)	938	(54.8%)	55.7% (46.6-64.9)
Croup -influenza-common cold and non-specified or multiple ARIs	1662	(65.3%)	58.9% (47.7-70.2)			882	(34.7%)	41.1% (29.8-52.3)
Acute otitis	501	(61.8%)	55.6% (45.2-66.1)	102	(12.6%)	208	(25.6%)	27.7% (21.5-34.0)
Acute sinusitis	56	(69.1%)	69.9% (54.0-85.9)	7	(8.6%)	18	(22.2%)	20.7% (7.3-34.0)
Pneumonia	100	(35.6%)	38.7% (27.3-50.1)	142	(50.5%)	39	(13.9%)	15.3% (8.4-22.1)
Total	3207	(52.1%)	46.9% (38.2-55.6)	676	(11.0%)	2274	(36.9%)	41.5% (33.1-49.9)

Table 6.- Adjusted proportions in each center of first choice and inadequate prescriptions, according to multiple logistic regression.

	1st Choice use		**Inadequate use**	
Centers	%	95%CI	%	95%CI
Hospital A	69.8	(66.3 - 73.0)	18.2	(15.9 - 20.8)
Hospital B	52.4	(29.1 - 62.9)	32.0	(28.9 - 35.2)
Hospital C	46.1	(39.0 - 53.2)	38.0	(31.6 - 44.8)
Hospital D	49.6	(45.3 - 54.0)	33.7	(30.0 - 37.6)
Hospital E	46.3	(41.6 - 51.1)	38.9	(34.7 - 43.4)
Hospital F	64.2	(60.2 - 68.1)	13.2	(11.0 - 15.6)
Hospital G	31.0	(23.6 - 39.5)	50.5	(42.3 - 58.8)
Hospital H	56.1	(51.4 - 60.7)	24.8	(21.4 - 28.4)
Hospital I	37.9	(33.8 - 42.1)	40.9	(37.1 - 44.7)
Hospital J	34.6	(27.4 - 42.6)	42.1	(34.5 - 50.1)
Hospital K	32.5	(25.3 - 40.6)	54.3	(46.2 - 62.2)